REMARKS/ARGUMENTS

The Pending Claims

Before entry of the preceding Amendments, Claims 1-10 are pending in the above-captioned application, directed to an animal model system for artificially inducing a heart arrhythmia.

Applicants' Amendment

Applicants have amended herein Claims 1 and 6-9 as further described below.

Applicants have added new Claims 11-21.

Support for new Claim 11 is found in the specification as originally filed, e.g., at page 8, lines 23-28.

Support for new Claim 12 is found in the specification, e.g., at page 8, line 23 through page 9, line 11; at page 6, line 30 through page 7, line 21; and Claims 1-2 and 4-5 as originally filed.

Support for new Claim 13 is found in the specification, e.g., at Claim 6, as originally filed.

Support for new Claim 14 is found in the specification, e.g., at Claim 7, as originally filed.

Support for new Claim 15 is found in the specification, e.g., at Claim 8, as originally filed.

Support for new Claim 16 is found in the specification, e.g., at Claim 9, as originally filed.

Support for new Claim 17 is found in the specification, e.g., at page 8, line 23 through page 9, line 11; at page 6, line 30 through page 7, line 21; and Claims 1-2 and 4-5 as originally filed.

Support for new Claim 18 is found in the specification, e.g., at Claim 6, as originally filed.

Support for new Claim 19 is found in the specification, e.g., at Claim 7, as originally filed.

Support for new Claim 20 is found in the specification, e.g., at Claim 8, as originally filed.

Support for new Claim 21 is found in the specification, e.g., at Claim 9, as originally filed.

No new matter is added by any of the amendments herein.

The Office Action and Applicant's Response

The Examiner noted in the Information Disclosure Statement, filed by Applicant December 27, 2001 under 37 C.F.R. § 1.98(d), that Other Art reference No. 1 (Schwartz, PJ *et al.* [1984]) was not considered, presumably because the Examiner was unable to locate it in the files of the USPTO. Applicant herewith submits a new copy of the Applicant-cited Schwartz *et al.* reference (Other Reference No. 1) and a new copy of Applicant's Form 1449, for the Examiner's consideration.

The Examiner acknowledged entry of Applicant's preliminary amendment and drawings received on December 27, 2001.

No claims were allowed. The following grounds of rejections were cited.

A. **Rejection under 35 U.S.C. § 101**

Claims 1-9 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

. . . The claims are directed to an animal model system for inducing a heart arrhythmia, the scope of which encompasses a human being. A human being is non-statutory subject matter. As such, the recitation of the limitation "non-human" would be remedial for the claims. See 1077 O.G. 24, April 21, 1987.

Applicant's amendment to Claims 1 and 6-9, deleting the phrase "animal test subject" and inserting therefor the phrase "canine test subject" is believed to overcome the cited ground of rejection.

Therefore, the Examiner is respectfully requested to withdraw the rejection of Claims 1-9 under 35 U.S.C. 101.

B. Rejections under 35 U.S.C. § 112

(1) The Examiner rejected Claims 1-9, under **35 U.S.C. §112, first paragraph**. The Examiner stated the following reasons:

> **. . . Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.**
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> **The specification has described a canine model system for artificially inducing heart arrhythmia. See throughout the specification. The specification however, has not described the other animals encompassed by the claims. There is no evidence on the record of a relationship between the structures of the animals embraced by the claims that would provide any reliable information about the structure of animals within the genus. There is no evidence on the record that the canine model had a known structural relationship to any other animals to be used as model systems of heart arrhythmia embraced by the claims, the specification discloses only a canine model and the art indicated that there is variation between the structures of the other animals to be used as model systems of heart arrhythmia. There is no evidence of record that would indicate that any of the other animals embraced by the claims, could even serve as model systems.**

Applicant's amendment to Claims 1 and 6-9, deleting the phrase "animal test subject" and inserting therefor the phrase "canine test subject" is believed to overcome the cited ground of rejection.

Therefore, Applicants respectfully request the Examiner to withdraw the rejection of Claims 1-9 on this ground.

(2) Claim 2 was rejected under **35 U.S.C. §112, first paragraph**.

> **. . . Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.**
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> **The neurotrophic vectors encompassed within the genus have not been disclosed. Based upon the prior art there is expected to be variation among the species neurotrophic vectors, because the structures of neurotrophic vectors would be expected to vary. The specification describes a method for practicing the claimed invention by administering nerve growth factor to stimulate myocardial hyperinnervation but does not describe methods for practicing the claimed invention by administering other neurotrophic vectors to stimulate myocardial hyperinnervation. There is no evidence on the record of a relationship between the structures of any neurotrophic vectors and nerve growth factor that would provide any reliable information about the structure of the other neurotrophic vectors within the genus. There is no evidence on the record that nerve growth factor had a known structural relationship to other neurotrophic vectors; the specification discloses only nerve growth factor of ruse in the claimed invention; the art indicated that there is variation between nerve growth factor and other neurotrophic vectors. There is no evidence of record that would indicate that any of the other neurotrophic vectors embraced by the claims would even be able to stimulate myocardial hyperinnervation. In view of the above considerations one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by member of the genus of neurotrophic vectors, because nerve growth factor is not representative of the claimed genus. Consequently, since Applicant was in possession of only methods requiring nerve growth factor and since the art recognized variation among neurotrophic vectors, nerve growth factor**

was not representative of the claimed genus. Therefore, Applicant was not in possession of the genus of neurotrophic vectors as encompassed by the claims. University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that to fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention."

Applicant strongly disagrees with the ground of rejection, because, based on the general knowledge in the art at the time of filing and the disclosures of Applicant's specification, the skilled artisan would be aware of other members of a genus of neurotrophic vectors, of which NGF is a member.

Applicant's specification teaches that in one embodiment of the invention "the left stellate ganglion is . . . infused with NGF, or other neurotrophic vector . . . for the purposes of stimulating nerve sprouting or other forms of hyperinnervation within the left stellate ganglion or within the vicinity thereof. Other suitable neurotrophic vectors include neurotrophic chemicals, substances, hormones, etc." (Specification at page 8, lines 25-29). Contrary to the Examiner's assertion, the skilled artisan would also have been aware of general knowledge in the art concerning structural, as well as functional, relatedness within the genus of neurotrophic vectors, i.e., neurotrophins, of which nerve growth factor (NGF) is a species. For example, Ibáñez *et al.* taught that "NGF belongs to a family of structurally and functionally related molecules, collectively known as neurotrophins, which includes three other members, brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3) and neurotrophin-4 (NT-4), also known as neurotrophin-5. All neurotrophins display both overlapping and specific sets of neurotrophic activities." (Ibáñez CF *et al.*, *Neurotrophin-4 is a target-derived neurotrophic factor for neurons of the trigeminal ganglion*, Development 117:1345-1353 [1993], at page 1345, second column, bridging paragraph through page 1346, first column, line 8; citations omitted; appended as **Exhibit A**). The skilled artisan would be aware that the neurotrophins (NGF, BDNF, NT-3, and NT-4/5) are dimeric molecules, which share approximately 50% sequence identity; and in some critical structural regions (e.g., their *trk* receptor-binding regions or subunit interfaces) share high sequence conservation throughout the neurotrophin family. (See, Robinson RC *et al.*, *Structure of the brain-derived neurotrophic factor/neurotrophin 3 heterodimer*, Biochemistry 34(13):4139-46 [1995], abstract appended as **Exhibit B**; Robinson RC *et al.*, *The structures of the neurotrophin 4 homodimer and the brain-derived neurotrophic factor/neurotrophin 4 heterodimer reveal a common Trk-binding site*, Protein Sci. 8(12):2589-97 [1999], abstract appended as **Exhibit C**). Thus, based on the disclosures of the specification and the general

knowledge in the art, it would have been apparent to the skilled artisan that Applicant was in possession of the claimed invention with respect to "neurotrophic vector," as recited in Claim 2.

Consequently, Applicant respectfully requests the Examiner to withdraw the rejection of Claim 2 on this ground.

(3) Claims 1-10 were also rejected under **35 U.S.C. §112, second paragraph**. The rejection as to Claim 10 is mooted by the cancellation of that claim. As to pending Claims 1-9, The Examiner asserted that

> **. . . Claim 1 is indefinite as written. The claim embraces surgical and/or chemical blocking of the coronary artery. The term "and/or" renders the claim indefinite because it is not clear which step, either chemical or surgical or both, is used to block the coronary artery. Correction is required. Claims 2-10 depend from claim 1.**

Claim 1 has been amended herein for greater clarity to delete the recitation of the expression "and/or", such that amended Claim 1 recites, *inter alia*, ". . . the anterior descending portion of the coronary artery of the heart of the animalcanine test subject being surgically *or* chemically blocked, *or both*, for inducing a myocardial infarction." The amendment is believed to overcome the rejection. Accordingly, the Examiner is respectfully requested to withdraw the rejection on this ground.

The Examiner further stated:

> **. . . Claim 6 is unclear as written. The claim is directed to an ICD that further applies techniques to prevent the occurrence of further arrhythmias. The claim is unclear because neither the specification or the art of record define techniques applied by an ICD. As such it is not known what is meant by techniques that are applied by an ICD. Clarification is required.**
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> **Claim 7 is unclear as written. The claim is directed to an ICD that further applied techniques to prevent the occurrence of ventricular arrhythmias. The claim is unclear because neither the specification nor the art of record define techniques applied by an ICD. As such it is not known what is meant by techniques that are applied by an ICD. Clarification is required.**

Applicant's specification provides guidance as to relevant ICD therapies for the prevention and treatment of cardiac arrhythmias, such as ventricular tachycardia (VT) and, as recited particularly in Claim 7, ventricular fibrillation (VF) of the heart (e.g., at page 1, line 25 through page 2, line 12; at page 6, line 30 through page 7, line 24; at page 9, lines 20-31; and at page 10, lines 3-21).

In addition, the skilled artisan would be aware of widely used ICD techniques for the prevention of VT and VF of the heart, as recited particularly in Claim 7. For example, Engelstein ED, *Prevention and Management of Chronic Heart Failure with Electrical Therapy*,

Am. J. Cardiol. 91(suppl):62F-73F (2003; copy appended as **Exhibit D**) reviews well known ICD therapies for the treatment and prevention of VF (see, e.g., page 64F, first column, last paragraph through page 68F, first column, line 5); the vast majority of the references cited in the Engelstein review were published pre-filing date (e.g., see page 64F, second column, through page 65F, second column, reviewing data from a number of randomized clinical trials for ICD therapies conducted during 1986-1999, including "Antiarrhythmics Versus Implantable Defibrillators" [AVID] trial, the "Cardiac Arrest Study Hamburg" [CASH], the "Canadian Implantable Defibrillator Study" [CIDS], the "Multicenter Automatic Defibrillator Implantation Trial" [MADIT], and the Multicenter Unsustained Tachycardia Trial [MUSTT]). The Engelstein review indicates that the general knowledge in the art was quite familiar with the clinical application of ICD to treating and preventing ventricular arrhythmias, including VT and VF.

Therefore, Applicant respectfully requests the Examiner to withdraw the rejection on this ground.

CONCLUSION

In view of the above amendments and remarks, it is submitted that this application is now ready for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney at (213) 896-6665.

Respectfully submitted,

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